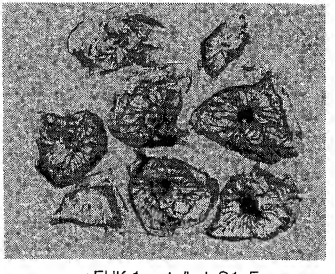
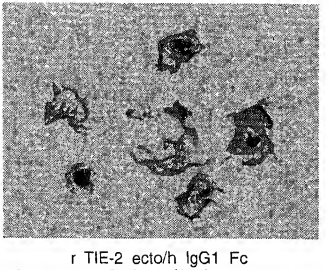
Fig.1A.



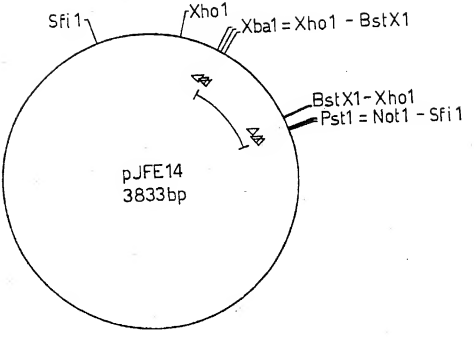
r EHK-1 ecto/h IgG1 Fc
Gelfoam (6ug)

Fig.1B.



r TIE-2 ecto/h IgG1 Fc
Gelfoam (6ug)

Fig.2


Sfi 1
Xho1
Xba1 = Xho1 - BstX1
BstX1 - Xho1
Pst1 = Not1 - Sfi 1
pJFE14
3833bp

Att. Docket No. REG 330G1Z
USSN: Not Yet Known
File Date: Filed Herewith
Applicant:Davis, et al.
Title: TIE-2 Ligands, Methods of Making and Uses Thereof

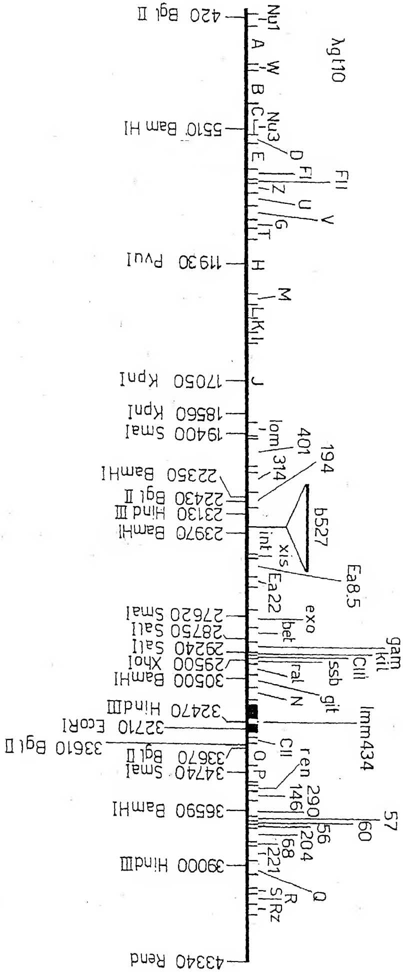


Fig.3.

Fig. 4A

```
          10         20         30         40         50         60         70         80
          *          *          *          *          *          *          *          *
CAGCTGACTCAGGCAGGCTCCATGCTGAACGGTCACACAGAGAGGAAACAATAAATCTCAGCTACTATGCAATAAATATC

          90         100        110        120        130        140        150        160
          *          *          *          *          *          *          *          *
TCAAGTTTTAACGAAGAAAAACATCATTGCAGTGAAATAAAAAATTTTAAAATTTTAGAACAAAGCTAACAAATGGCTAG

          170        180        190        200        210        220        230        240
          *          *          *          *          *          *          *          *
TTTTCTATGATTCTTCTTCAAACGCTTTCTTTGAGGGGGAAAGAGTCAAACAAACAAGCAGTTTTACCTGAAATAAAGAA

          250        260        270        280        290        300        310
          *          *          *          *          *          *          *
CTAGTTTTAGAGGTCAGAAGAAAGGAGCAAGTTTTGCGAGAGGCACGGAAGGAGTGTGCTGGCAGTACA ATG ACA GTT
                                                                          M   T   V>

320        330        340        350        360        370
*          *          *          *          *          *
TTC CTT TCC TTT GCT TTC CTC GCT GCC ATT CTG ACT CAC ATA GGG TGC AGC AAT CAG CGC
 F   L   S   F   A   F   L   A   A   I   L   T   H   I   G   C   S   N   Q   R>

380        390        400        410        420        430
*          *          *          *          *          *
CGA AGT CCA GAA AAC AGT GGG AGA AGA TAT AAC CGG ATT CAA CAT GGG CAA TGT GCC TAC
 R   S   P   E   N   S   G   R   R   Y   N   R   I   Q   H   G   Q   C   A   Y>
```

Fig. 4B

```
                440                 450                 460                 470                 480                 490
                 *                   *                   *                   *                   *                   *
ACT TTC ATT CTT CCA GAA CAC GAT GGC AAC TGT CGT GAG AGT ACG ACA GAC CAG TAC AAC
 T   F   I   L   P   E   H   D   G   N   C   R   E   S   T   T   D   Q   Y   N>

500                 510                 520                 530                 540                 550
 *                   *                   *                   *                   *                   *
ACA AAC GCT CTG CAG AGA GAT GCT CCA CAC GTG GAA CCG GAT TTC TCT TCC CAG AAA CTT
 T   N   A   L   Q   R   D   A   P   H   V   E   P   D   F   S   S   Q   K   L>

560                 570                 580                 590                 600                 610
 *                   *                   *                   *                   *                   *
CAA CAT CTG GAA CAT GTG ATG GAA AAT TAT ACT CAG TGG CTG CAA AAA CTT GAG AAT TAC
 Q   H   L   E   H   V   M   E   N   Y   T   Q   W   L   Q   K   L   E   N   Y>

620                 630                 640                 650                 660                 670
 *                   *                   *                   *                   *                   *
ATT GTG GAA AAC ATG AAG TCG GAG ATG GCC CAG ATA CAG CAG AAT GCA GTT CAG AAC CAC
 I   V   E   N   M   K   S   E   M   A   Q   I   Q   Q   N   A   V   Q   N   H>

680                 690                 700                 710                 720                 730
 *                   *                   *                   *                   *                   *
ACG GCT ACC ATG CTG GAG ATA GGA ACC AGC CTC CTC TCT CAG ACT GCA GAG CAG ACC AGA
 T   A   T   M   L   E   I   G   T   S   L   L   S   Q   T   A   E   Q   T   R>
```

Fig. 4C

```
740                 750                 760                 770                 780                 790
*                   *                   *                   *                   *                   *
AAG CTG ACA GAT GTT GAG ACC CAG GTA CTA AAT CAA ACT TCT CGA CTT GAG ATA CAG CTG
K   L   T   D   V   E   T   Q   V   L   N   Q   T   S   R   L   E   I   Q   L>

800                 810                 820                 830                 840                 850
*                   *                   *                   *                   *                   *
CTG GAG AAT TCA TTA TCC ACC TAC AAG CTA GAG AAG CAA CTT CTT CAA CAG ACA AAT GAA
L   E   N   S   L   S   T   Y   K   L   E   K   Q   L   L   Q   Q   T   N   E>

860                 870                 880                 890                 900                 910
*                   *                   *                   *                   *                   *
ATC TTG AAG ATC CAT GAA AAA AAC AGT TTA TTA GAA CAT AAA ATC TTA GAA ATG GAA GGA
I   L   K   I   H   E   K   N   S   L   L   E   H   K   I   L   E   M   E   G>

920                 930                 940                 950                 960                 970
*                   *                   *                   *                   *                   *
AAA CAC AAG GAA GAG TTG GAC ACC TTA AAG GAA GAG AAA GAG AAC CTT CAA GGC TTG GTT
K   H   K   E   E   L   D   T   L   K   E   E   K   E   N   L   Q   G   L   V>

980                 990                 1000                1010                1020                1030
*                   *                   *                   *                   *                   *
ACT CGT CAA ACA TAT ATA ATC CAG GAG CTG GAA AAG CAA TTA AAC AGA GCT ACC ACC AAC
T   R   Q   T   Y   I   I   Q   E   L   E   K   Q   L   N   R   A   T   T   N>
```

Fig. 4D

```
1040          1050          1060          1070          1080          1090
 *             *             *             *             *             *
 AAC AGT GTC CTT CAG AAG CAG CAA CTG GAG CTG ATG GAC ACA GTC CAC AAC CTT GTC AAT
  N   S   V   L   Q   K   Q   Q   L   E   L   M   D   T   V   H   N   L   V   N>

1100          1110          1120          1130          1140          1150
 *             *             *             *             *             *
 CTT TGC ACT AAA GAA GGT GTT TTA CTA AGG GGA GGA AAA AGA GAG GAA GAG AAA CCA TTT
  L   C   T   K   E   G   V   L   L   K   G   G   K   R   E   E   E   K   P   F>

1160          1170          1180          1190          1200          1210
 *             *             *             *             *             *
 AGA GAC TGT GCA GAT GTA TAT CAA GCT GGT TTT AAT AAA AGT GGA ATC TAC ACT ATT TAT
  R   D   C   A   D   V   Y   Q   A   G   F   N   K   S   G   I   Y   T   I   Y>

1220          1230          1240          1250          1260          1270
 *             *             *             *             *             *
 ATT AAT AAT ATG CCA GAA CCC AAA AAG GTG TTT TGC AAT ATG GAT GTC AAT GGG GGA GGT
  I   N   N   M   P   E   P   K   K   V   F   C   N   M   D   V   N   G   G   G>

1280          1290          1300          1310          1320          1330
 *             *             *             *             *             *
 TGG ACT GTA ATA CAA CAT CGT GAA GAT GGA AGT CTA GAT TTC CAA AGA GGC TGG AAG GAA
  W   T   V   I   Q   H   R   E   D   G   S   L   D   F   Q   R   G   W   K   E>

1340          1350          1360          1370          1380          1390
 *             *             *             *             *             *
 TAT AAA ATG GGT TTT GGA AAT CCC TCC GGT GAA TAT TGG CTG GGG AAT GAG TTT ATT TTT
  Y   K   M   G   F   G   N   P   S   G   E   Y   W   L   G   N   E   F   I   F>
```

Fig. 4E

```
1400                1410                1420                1430                1440                1450
 *                   *                   *                   *                   *                   *
 GCC ATT ACC AGT CAG AGG CAG TAC ATG CTA AGA ATT GAG TTA ATG GAC TGG GAA GGG AAC
  A   I   T   S   Q   R   Q   Y   M   L   R   I   E   L   M   D   W   E   G   N>

1460                1470                1480                1490                1500                1510
 *                   *                   *                   *                   *                   *
 CGA GCC TAT TCA CAG TAT GAC AGA TTC CAC ATA GGA AAT GAA AAG CAA AAC TAT AGG TTG
  R   A   Y   S   Q   Y   D   R   F   H   I   G   N   E   K   Q   N   Y   R   L>

1520                1530                1540                1550                1560                1570
 *                   *                   *                   *                   *                   *
 TAT TTA AAA GGT CAC ACT GGG ACA GCA GGA AAA CAG AGC AGC CTG ATC TTA CAC GGT GCT
  Y   L   K   G   H   T   G   T   A   G   K   Q   S   S   L   I   L   H   G   A>

1580                1590                1600                1610                1620                1630
 *                   *                   *                   *                   *                   *
 GAT TTC AGC ACT AAA GAT GCT GAT AAT GAC AAC TGT ATG TGC AAA TGT GCC CTC ATG TTA
  D   F   S   T   K   D   A   D   N   D   N   C   M   C   K   C   A   L   M   L>

1640                1650                1660                1670                1680                1690
 *                   *                   *                   *                   *                   *
 ACA GGA GGA TGG TGG TTT GAT GCT TGT GGC CCC TCC AAT CTA AAT GGA ATG TTC TAT ACT
  T   G   G   W   W   F   D   A   C   G   P   S   N   L   N   G   M   F   Y   T>
```

Fig. 4F

```
1700                1710                  1720               1730               1740                1750
 *                   *                     *                  *                  *                   *
GCG GGA CAA AAC CAT GGA AAA CTG AAT GGG ATA AAG TGG CAC TAC TTC AAA GGG CCC AGT
 A   G   Q   N   H   G   K   L   N   G   I   K   W   H   Y   F   K   G   P   S>

      1760                1770                1780              1790              1800
 *                   *                   *                  *                  *
TAC TCC TTA CGT TCC ACA ACT ATG ATG ATT CGA CCT TTA GAT TTT TGA
 Y   S   L   R   S   T   T   M   M   I   R   P   L   D   F   *>

  1810           1820           1830           1840
   *              *              *              *
AAGCGCAATGTCAGAAGCGATTATGAAAGCAACA

        1850           1860           1870           1880           1890           1900           1910           1920
         *              *              *              *              *              *              *              *
AAGAAATCCGGAGAAGCTGCCAGGTGAGAAACTGTTTGAAAACTTCAGAAGCAAACAATATTGTCTCCCTTCCAGCAATA

        1930           1940           1950           1960           1970           1980           1990           2000
         *              *              *              *              *              *              *              *
AGTGGTAGTTATGTGAAGTCACCAAGGTTCTTGACCGTGAATCTGGAGCCGTTTGAGTTCACAAGAGTCTCTACTTGGGG

        2010           2020           2030           2040           2050           2060           2070           2080
         *              *              *              *              *              *              *              *
TGACAGTGCTCACGTGGCTCGACTATAGAAAACTCCACTGACTGTCGGGCTTTAAAAAGGGAAGAAACTGCTGAGCTTGC

        2090           2100           2110           2120           2130           2140
         *              *              *              *              *              *
TGTGCTTCAAACTACTACTGGACCTTATTTTGGAACTATGGTAGCCAGATGATAAATATGGTTAATTTC
```

Fig. 5A

```
         10         20         30         40         50         60         70         80
         *          *          *          *          *          *          *          *
CAGCTGACTCAGGCAGGCTCCATGCTGAACGGTCACACAGAGAGGAAACAATAAATCTCAGCTACTATGCAATAAATATC

         90         100        110        120        130        140        150        160
         *          *          *          *          *          *          *          *
TCAAGTTTTAACGAAGAAAAACATCATTGCAGTGAAATAAAAAATTTTAAAATTTTAGAACAAAGCTAACAAATGGCTAG

         170        180        190        200        210        220        230        240
         *          *          *          *          *          *          *          *
TTTTCTATGATTCTTCTTCAAACGCTTTCTTTGAGGGGAAAGAGTCAAACAAACAAGCAGTTTTACCTGAAATAAAGAA

         250        260        270        280        290        300        310
         *          *          *          *          *          *          *
CTAGTTTTAGAGGTCAGAAGAAAGGAGCAAGTTTTGCGAGAGGCACGGAAGGAGTGTGCTGGCAGTACA ATG ACA GTT
                                                                        M   T   V>

320        330        340        350        360        370
*          *          *          *          *          *
TTC CTT TCC TTT GCT TTC CTC GCT GCC ATT CTG ACT CAC ATA GGG TGC AGC AAT CAG CGC
 F   L   S   F   A   F   L   A   A   I   L   T   H   I   G   C   S   N   Q   R>

380        390        400        410        420        430
*          *          *          *          *          *
CGA AGT CCA GAA AAC AGT GGG AGA AGA TAT AAC CGG ATT CAA CAT GGG CAA TGT GCC TAC
 R   S   P   E   N   S   G   R   R   Y   N   R   I   Q   H   G   Q   C   A   Y>
```

Fig. 5B

```
440         450         460         470         480         490
*           *           *           *           *           *
ACT TTC ATT CTT CCA GAA CAC GAT GGC AAC TGT CGT GAG AGT ACG ACA GAC CAG TAC AAC
T   F   I   L   P   E   H   D   G   N   C   R   E   S   T   T   D   Q   Y   N>

500         510         520         530         540         550
*           *           *           *           *           *
ACA AAC GCT CTG CAG AGA GAT GCT CCA CAC GTG GAA CCG GAT TTC TCT TCC CAG AAA CTT
T   N   A   L   Q   R   D   A   P   H   V   E   P   D   F   S   S   Q   K   L>

560         570         580         590         600         610
*           *           *           *           *           *
CAA CAT CTG GAA CAT GTG ATG GAA AAT TAT ACT CAG TGG CTG CAA AAA CTT GAG AAT TAC
Q   H   L   E   H   V   M   E   N   Y   T   Q   W   L   Q   K   L   E   N   Y>

620         630         640         650         660         670
*           *           *           *           *           *
ATT GTG GAA AAC ATG AAG TCG GAG ATG GCC CAG ATA CAG CAG AAT GCA GTT CAG AAC CAC
I   V   E   N   M   K   S   E   M   A   Q   I   Q   Q   N   A   V   Q   N   H>

680         690         700         710         720         730
*           *           *           *           *           *
ACG GCT ACC ATG CTG GAG ATA GGA ACC AGC CTC CTC TCT CAG ACT GCA GAG CAG ACC AGA
T   A   T   M   L   E   I   G   T   S   L   L   S   Q   T   A   E   Q   T   R>

740         750         760         770         780         790
*           *           *           *           *           *
AAG CTG ACA GAT GTT GAG ACC CAG GTA CTA AAT CAA ACT TCT CGA CTT GAG ATA CAG CTG
K   L   T   D   V   E   T   Q   V   L   N   Q   T   S   R   L   E   I   Q   L>
```

Fig. 5C

```
800                 810                 820                 830                 840                 850
*                   *                   *                   *                   *                   *
CTG GAG AAT TCA TTA TCC ACC TAC AAG CTA GAG AAG CAA CTT CTT CAA CAG ACA AAT GAA
 L   E   N   S   L   S   T   Y   K   L   E   K   Q   L   L   Q   Q   T   N   E>

860                 870                 880                 890                 900                 910
*                   *                   *                   *                   *                   *
ATC TTG AAG ATC CAT GAA AAA AAC AGT TTA TTA GAA CAT AAA ATC TTA GAA ATG GAA GGA
 I   L   K   I   H   E   K   N   S   L   L   E   H   K   I   L   E   M   E   G>

920                 930                 940                 950                 960                 970
*                   *                   *                   *                   *                   *
AAA CAC AAG GAA GAG TTG GAC ACC TTA AAG GAA GAG AAA GAG AAC CTT CAA GGC TTG GTT
 K   H   K   E   E   L   D   T   L   K   E   E   K   E   N   L   Q   G   L   V>

980                 990                1000                1010                1020                1030
*                   *                   *                   *                   *                   *
ACT CGT CAA ACA TAT ATA ATC CAG GAG CTG GAA AAG CAA TTA AAC AGA GCT ACC ACC AAC
 T   R   Q   T   Y   I   I   Q   E   L   E   K   Q   L   N   R   A   T   T   N>

1040                1050                1060                1070                1080                1090
*                   *                   *                   *                   *                   *
AAC AGT GTC CTT CAG AAG CAG CAA CTG GAG CTG ATG GAC ACA GTC CAC AAC CTT GTC AAT
 N   S   V   L   Q   K   Q   Q   L   E   L   M   D   T   V   H   N   L   V   N>

1100                1110                1120                1130                1140                1150
*                   *                   *                   *                   *                   *
CTT TGC ACT AAA GAA GTT TTA CTA AAG GGA GGA AAA AGA GAG GAA GAG AAA CCA TTT AGA
 L   C   T   K   E   V   L   L   K   G   G   K   R   E   E   E   K   P   F   R>
```

Fig. 5D

```
1160            1170            1180            1190            1200            1210
 *               *               *               *               *               *
GAC TGT GCA GAT GTA TAT CAA GCT GGT TTT AAT AAA AGT GGA ATC TAC ACT ATT TAT ATT
 D   C   A   D   V   Y   Q   A   G   F   N   K   S   G   I   Y   T   I   Y   I>

1220            1230            1240            1250            1260            1270
 *               *               *               *               *               *
AAT AAT ATG CCA GAA CCC AAA AAG GTG TTT TGC AAT ATG GAT GTC AAT GGG GGA GGT TGG
 N   N   M   P   E   P   K   K   V   F   C   N   M   D   V   N   G   G   G   W>

1280            1290            1300            1310            1320            1330
 *               *               *               *               *               *
ACT GTA ATA CAA CAT CGT GAA GAT GGA AGT CTA GAT TTC CAA AGA GGC TGG AAG GAA TAT
 T   V   I   Q   H   R   E   D   G   S   L   D   F   Q   R   G   W   K   E   Y>

1340            1350            1360            1370            1380            1390
 *               *               *               *               *               *
AAA ATG GGT TTT GGA AAT CCC TCC GGT GAA TAT TGG CTG GGG AAT GAG TTT ATT TTT GCC
 K   M   G   F   G   N   P   S   G   E   Y   W   L   G   N   E   F   I   F   A>

1400            1410            1420            1430            1440            1450
 *               *               *               *               *               *
ATT ACC AGT CAG AGG CAG TAC ATG CTA AGA ATT GAG TTA ATG GAC TGG GAA GGG AAC CGA
 I   T   S   Q   R   Q   Y   M   L   R   I   E   L   M   D   W   E   G   N   R>

1460            1470            1480            1490            1500            1510
 *               *               *               *               *               *
GCC TAT TCA CAG TAT GAC AGA TTC CAC ATA GGA AAT GAA AAG CAA AAC TAT AGG TTG TAT
 A   Y   S   Q   Y   D   R   F   H   I   G   N   E   K   Q   N   Y   R   L   Y>
```

Fig. 5E

```
1520          1530          1540          1550          1560          1570
 *             *             *             *             *             *
TTA AAA GGT CAC ACT GGG ACA GCA GGA AAA CAG AGC AGC CTG ATC TTA CAC GGT GCT GAT
 L   K   G   H   T   G   T   A   G   K   Q   S   S   L   I   L   H   G   A   D>

1580          1590          1600          1610          1620          1630
 *             *             *             *             *             *
TTC AGC ACT AAA GAT GCT GAT AAT GAC AAC TGT ATG TGC AAA TGT GCC CTC ATG TTA ACA
 F   S   T   K   D   A   D   N   D   N   C   M   C   K   C   A   L   M   L   T>

1640          1650          1660          1670          1680          1690
 *             *             *             *             *             *
GGA GGA TGG TGG TTT GAT GCT TGT GGC CCC TCC AAT CTA AAT GGA ATG TTC TAT ACT GCG
 G   G   W   W   F   D   A   C   G   P   S   N   L   N   G   M   F   Y   T   A>

1700          1710          1720          1730          1740          1750
 *             *             *             *             *             *
GGA CAA AAC CAT GGA AAA CTG AAT GGG ATA AAG TGG CAC TAC TTC AAA GGG CCC AGT TAC
 G   Q   N   H   G   K   L   N   G   I   K   W   H   Y   F   K   G   P   S   Y>

1760          1770          1780          1790          1800
 *             *             *             *             *
TCC TTA CGT TCC ACA ACT ATG ATG ATT CGA CCT TTA GAT TTT TGA
 S   L   R   S   T   T   M   M   I   R   P   L   D   F   *>
```

Fig. 5F

```
      1810      1820      1830      1840
         *         *         *         *
AAGCGCAATGTCAGAAGCGATTATGAAAGCAACAAAG

        1850      1860      1870      1880      1890      1900      1910      1920
           *         *         *         *         *         *         *         *
AAATCCGGAGAAGCTGCCAGGTGAGAAACTGTTTGAAAACTTCAGAAGCAAACAATATTGTCTCCCTTCCAGCAATAAGT

        1930      1940      1950      1960      1970      1980      1990      2000
           *         *         *         *         *         *         *         *
GGTAGTTATGTGAAGTCACCAAGGTTCTTGACCGTGAATCTGGAGCCGTTTGAGTTCACAAGAGTCTCTACTTGGGGTGA

        2010      2020      2030      2040      2050      2060      2070      2080
           *         *         *         *         *         *         *         *
CAGTGCTCACGTGGCTCGACTATAGAAAACTCCACTGACTGTCGGGCTTTAAAAAGGGAAGAAACTGCTGAGCTTGCTGT

        2090      2100      2110      2120      2130      2140
           *         *         *         *         *         *
GCTTCAAACTACTACTGGACCTTATTTTGGAACTATGGTAGCCAGATGATAAATATGGTTAATTTC
```

Fig. 6A

```
          10         20         30         40         50         60         70         80
          *          *          *          *          *          *          *          *
GAATTCCTGGGTTGGTGTTTATCTCCTCCCAGCCTTGAGGGAGGGAACAACACTGTAGGATCTGGGGAGAGAGGAACAAA

          90         100        110        120        130        140        150        160
          *          *          *          *          *          *          *          *
GGACCGTGAAAGCTGCTCTGTAAAAGCTGACACAGCCCTCCCAAGTGAGCAGGACTGTTCTTCCCACTGCAATCTGACAG

          170        180        190        200        210        220        230        240
          *          *          *          *          *          *          *          *
TTTACTGCATGCCTGGAGAGAACACAGCAGTAAAAACCAGGTTTGCTACTGGAAAAAGAGGAAAGAGAAGACTTTCATTG

          250        260        270        280        290        300        310        320
          *          *          *          *          *          *          *          *
ACGGACCCAGCCATGGCAGCGTAGCAGCCCTGCGTTTCAGACGGCAGCAGCTCGGGACTCTGGACGTGTGTTTGCCCTCA

          330        340        350        360        370        380
          *          *          *          *          *          *
AGTTTGCTAAAGCTGCTGGTTTATTACTGAAGAAAGA ATG TGG CAG ATT GTT TTC TTT ACT CTG AGC TGT
                                        M   W   Q   I   V   F   F   T   L   S   C>

390        400        410        420        430        440
*          *          *          *          *          *
GAT CTT GTC TTG GCC GCA GCC TAT AAC AAC TTT CGG AAG AGC ATG GAC AGC ATA GGA AAG
 D   L   V   L   A   A   A   Y   N   N   F   R   K   S   M   D   S   I   G   K>

450        460        470        480        490        500
*          *          *          *          *          *
AAG CAA TAT CAG GTC CAG CAT GGG TCC TGC AGC TAC ACT TTC CTC CTG CCA GAG ATG GAC
 K   Q   Y   Q   V   Q   H   G   S   C   S   Y   T   F   L   L   P   E   M   D>
```

Fig. 6B

```
510               520               530               540               550               560
 *                 *                 *                 *                 *                 *
 AAC TGC CGC TCT TCC TCC AGC CCC TAC GTG TCC AAT GCT GTG CAG AGG GAC GCG CCG CTC
  N   C   R   S   S   S   S   P   Y   V   S   N   A   V   Q   R   D   A   P   L>

570               580               590               600               610               620
 *                 *                 *                 *                 *                 *
 GAA TAC GAT GAC TCG GTG CAG AGG CTG CAA GTG CTG GAG AAC ATC ATG GAA AAC AAC ACT
  E   Y   D   D   S   V   Q   R   L   Q   V   L   E   N   I   M   E   N   N   T>

630               640               650               660               670               680
 *                 *                 *                 *                 *                 *
 CAG TGG CTA ATG AAG CTT GAG AAT TAT ATC CAG GAC AAC ATG AAG AAA GAA ATG GTA GAG
  Q   W   L   M   K   L   E   N   Y   I   Q   D   N   M   K   K   E   M   V   E>

690               700               710               720               730               740
 *                 *                 *                 *                 *                 *
 ATA CAG CAG AAT GCA GTA CAG AAC CAG ACG GCT GTG ATG ATA GAA ATA GGG ACA AAC CTG
  I   Q   Q   N   A   V   Q   N   Q   T   A   V   M   I   E   I   G   T   N   L>

750               760               770               780               790               800
 *                 *                 *                 *                 *                 *
 TTG AAC CAA ACA GCT GAG CAA ACG CGG AAG TTA ACT GAT GTG GAA GCC CAA GTA TTA AAT
  L   N   Q   T   A   E   Q   T   R   K   L   T   D   V   E   A   Q   V   L   N>

810               820               830               840               850               860
 *                 *                 *                 *                 *                 *
 CAG ACC ACG AGA CTT GAA CTT CAG CTC TTG GAA CAC TCC CTC TCG ACA AAC AAA TTG GAA
  Q   T   T   R   L   E   L   Q   L   L   E   H   S   L   S   T   N   K   L   E>
```

Att. Docket No. REG 3306IZ
USSN: Not Yet Known
File Date: Filed Herewith
Applicant: Davis, et al.
Title: TIE-2 Ligands, Methods of Making and Uses Thereof

Fig. 6C

```
870              880              890              900              910              920
 *                *                *                *                *                *
 AAA CAG ATT TTG GAC CAG ACC AGT GAA ATA AAC AAA TTG CAA GAT AAG AAC AGT TTC CTA
  K   Q   I   L   D   Q   T   S   E   I   N   K   L   Q   D   K   N   S   F   L>

930              940              950              960              970              980
 *                *                *                *                *                *
 GAA AAG AAG GTG CTA GCT ATG GAA GAC AAG CAC ATC ATC CAA CTA CAG TCA ATA AAA GAA
  E   K   K   V   L   A   M   E   D   K   H   I   I   Q   L   Q   S   I   K   E>

990             1000             1010             1020             1030             1040
 *                *                *                *                *                *
 GAG AAA GAT CAG CTA CAG GTG TTA GTA TCC AAG CAA AAT TCC ATC ATT GAA GAA CTA GAA
  E   K   D   Q   L   Q   V   L   V   S   K   Q   N   S   I   I   E   E   L   E>

1050            1060             1070             1080             1090             1100
 *                *                *                *                *                *
 AAA AAA ATA GTG ACT GCC ACG GTG AAT AAT TCA GTT CTT CAA AAG CAG CAA CAT GAT CTC
  K   K   I   V   T   A   T   V   N   N   S   V   L   Q   K   Q   Q   H   D   L>

1110            1120             1130             1140             1150             1160
 *                *                *                *                *                *
 ATG GAG ACA GTT AAT AAC TTA CTG ACT ATG ATG TCC ACA TCA AAC TCA GCT AAG GAC CCC
  M   E   T   V   N   N   L   L   T   M   M   S   T   S   N   S   A   K   D   P>

1170            1180             1190             1200             1210             1220
 *                *                *                *                *                *
 ACT GTT GCT AAA GAA GAA CAA ATC AGC TTC AGA GAC TGT GCT GAA GTA TTC AAA TCA GGA
  T   V   A   K   E   E   Q   I   S   F   R   D   C   A   E   V   F   K   S   G>
```

Fig. 6D

```
1230            1240            1250              1260             1270            1280
 *               *               *                 *                *               *
 CAC ACC ACA AAT GGC ATC TAC ACG TTA ACA TTC CCT AAT TCT ACA GAA GAG ATC AAG GCC
  H   T   T   N   G   I   Y   T   L   T   F   P   N   S   T   E   E   I   K   A>

1290            1300            1310              1320             1330            1340
 *               *               *                 *                *               *
 TAC TGT GAC ATG GAA GCT GGA GGA GGC GGG TGG ACA ATT ATT CAG CGA CGT GAG GAT GGC
  Y   C   D   M   E   A   G   G   G   G   W   T   I   I   Q   R   R   E   D   G>

1350            1360            1370              1380             1390            1400
 *               *               *                 *                *               *
 AGC GTT GAT TTT CAG AGG ACT TGG AAA GAA TAT AAA GTG GGA TTT GGT AAC CCT TCA GGA
  S   V   D   F   Q   R   T   W   K   E   Y   K   V   G   F   G   N   P   S   G>

1410            1420            1430              1440             1450            1460
 *               *               *                 *                *               *
 GAA TAT TGG CTG GGA AAT GAG TTT GTT TCG CAA CTG ACT AAT CAG CAA CGC TAT GTG CTT
  E   Y   W   L   G   N   E   F   V   S   Q   L   T   N   Q   Q   R   Y   V   L>

1470            1480            1490              1500             1510            1520
 *               *               *                 *                *               *
 AAA ATA CAC CTT AAA GAC TGG GAA GGG AAT GAG GCT TAC TCA TTG TAT GAA CAT TTC TAT
  K   I   H   L   K   D   W   E   G   N   E   A   Y   S   L   Y   E   H   F   Y>

1530            1540            1550              1560             1570            1580
 *               *               *                 *                *               *
 CTC TCA AGT GAA GAA CTC AAT TAT AGG ATT CAC CTT AAA GGA CTT ACA GGG ACA GCC GGC
  L   S   S   E   E   L   N   Y   R   I   H   L   K   G   L   T   G   T   A   G>
```

Fig. 6E

```
1590          1600          1610          1620          1630          1640
 *             *             *             *             *             *
 AAA ATA AGC AGC ATC AGC CAA CCA GGA AAT GAT TTT AGC ACA AAG GAT GGA GAC AAC GAC
  K   I   S   S   I   S   Q   P   G   N   D   F   S   T   K   D   G   D   N   D>

1650          1660          1670          1680          1690          1700
 *             *             *             *             *             *
 AAA TGT ATT TGC AAA TGT TCA CAA ATG CTA ACA GGA GGC TGG TGG TTT GAT GCA TGT GGT
  K   C   I   C   K   C   S   Q   M   L   T   G   G   W   W   F   D   A   C   G>

1710          1720          1730          1740          1750          1760
 *             *             *             *             *             *
 CCT TCC AAC TTG AAC GGA ATG TAC TAT CCA CAG AGG CAG AAC ACA AAT AAG TTC AAC GGC
  P   S   N   L   N   G   M   Y   Y   P   Q   R   Q   N   T   N   K   F   N   G>

1770          1780          1790          1800          1810          1820
 *             *             *             *             *             *
 ATT AAA TGG TAC TAC TGG AAA GGC TCA GGC TAT TCG CTC AAG GCC ACA ACC ATG ATG ATC
  I   K   W   Y   Y   W   K   G   S   G   Y   S   L   K   A   T   T   M   M   I>

1830          1840
 *             *
 CGA CCA GCA GAT TTC
  R   P   A   D   F>

  1850          1860          1870          1880          1890          1900          1910          1920
   *             *             *             *             *             *             *             *
TAAACATCCCAGTCCACCTGAGGAACTGTCTCGAACTATTTTCAAAGACTTAAGCCCAGTGCACTGAAAGTCACGG
```

Fig. 6F

```
      1930        1940        1950        1960        1970        1980        1990        2000
       *           *           *           *           *           *           *           *
CTGCGCACTGTGTCCTCTTCCACCACAGAGGGCGTGTGCTCGGTGCTGACGGGACCCACATGCTCCAGATTAGAGCCTGT

       2010        2020        2030        2040        2050        2060        2070        2080
        *           *           *           *           *           *           *           *
AAACTTTATCACTTAAACTTGCATCACTTAACGGACCAAAGCAAGACCCTAAACATCCATAATTGTGATTAGACAGAACA

       2090        2100        2110        2120        2130        2140        2150        2160
        *           *           *           *           *           *           *           *
CCTATGCAAAGATGAACCCGAGGCTGAGAATCAGACTGACAGTTTACAGACGCTGCTGTCACAACCAAGAATGTTATGTG

       2170        2180        2190        2200        2210        2220        2230        2240
        *           *           *           *           *           *           *           *
CAAGTTTATCAGTAAATAACTGGAAAACAGAACACTTATGTTATACAATACAGATCATCTTGGAACTGCATTCTTCTGAG

       2250        2260        2270        2280
        *           *           *           *
CACTGTTTATACACTGTGTAAATACCCATATGTCCTGAATTC
```

Fig.7.

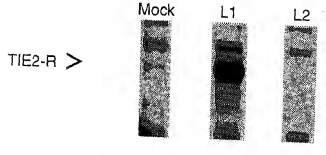


Fig.8.

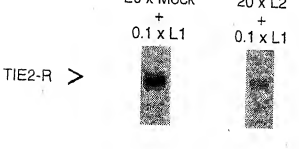


Fig.9.

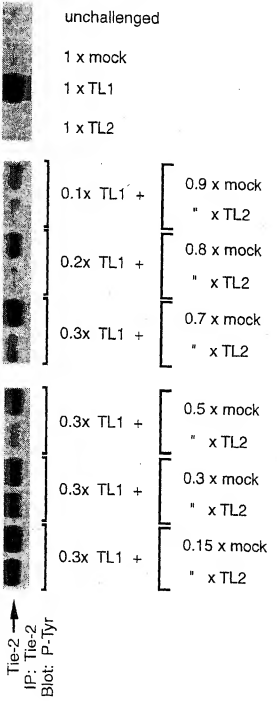

unchallenged
1 x mock
1 x TL1
1 x TL2
0.1x TL1 +
0.9 x mock
" x TL2
0.2x TL1 +
0.8 x mock
" x TL2
0.3x TL1 +
0.7 x mock
" x TL2
0.3x TL1 +
0.5 x mock
" x TL2
0.3x TL1 +
0.3 x mock
" x TL2
0.3x TL1 +
0.15 x mock
" x TL2
Tie-2
IP: Tie-2
Blot: P-Tyr

Fig.10.

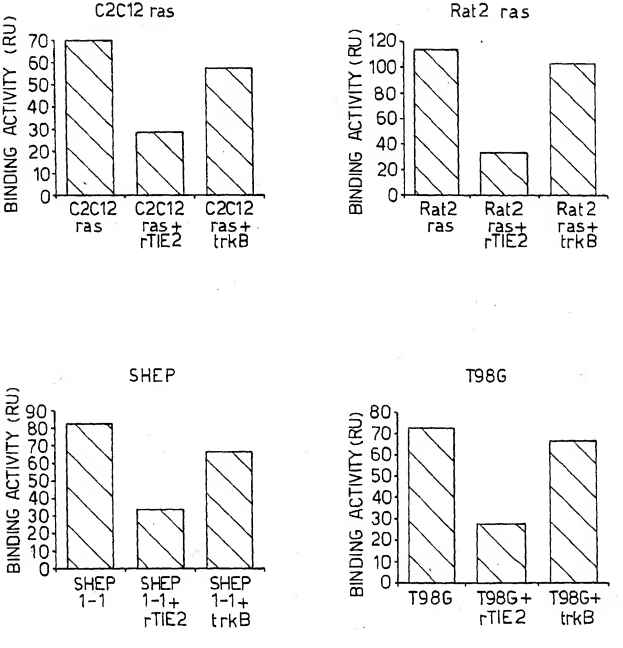
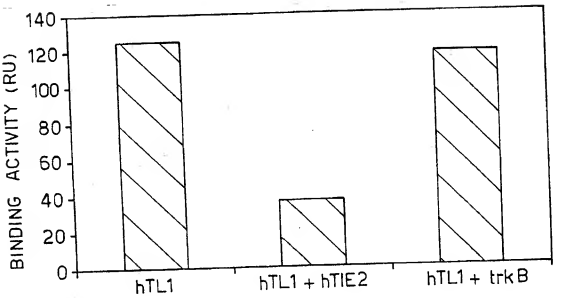

C2C12 ras
BINDING ACTIVITY (RU)
0
10
20
30
40
50
60
70
C2C12 ras
C2C12 ras+ rTIE2
C2C12 ras+ trkB
Rat2 ras
BINDING ACTIVITY (RU)
0
20
40
60
80
100
120
Rat2 ras
Rat2 ras+ rTIE2
Rat2 ras+ trkB
SHEP
BINDING ACTIVITY (RU)
0
10
20
30
40
50
60
70
80
90
SHEP 1-1
SHEP 1-1+ rTIE2
SHEP 1-1+ trkB
T98G
BINDING ACTIVITY (RU)
0
10
20
30
40
50
60
70
80
T98G
T98G+ rTIE2
T98G+ trkB

Fig.11.


BINDING ACTIVITY (RU)
140
120
100
80
60
40
20
0
hTL1
hTL1 + hTIE2
hTL1 + trk B

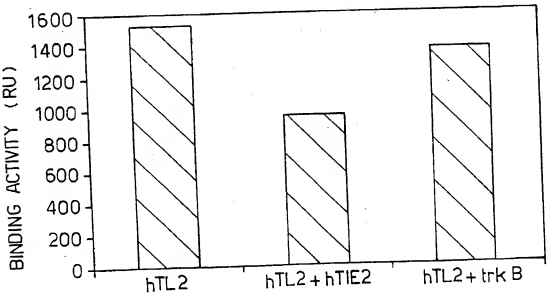

BINDING ACTIVITY (RU)
1600
1400
1200
1000
800
600
400
200
0
hTL2
hTL2 + hTIE2
hTL2 + trk B

Fig.12.

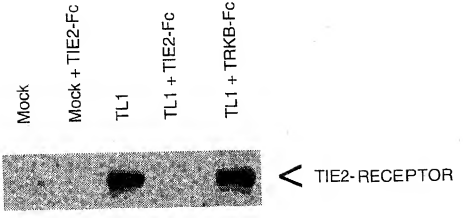
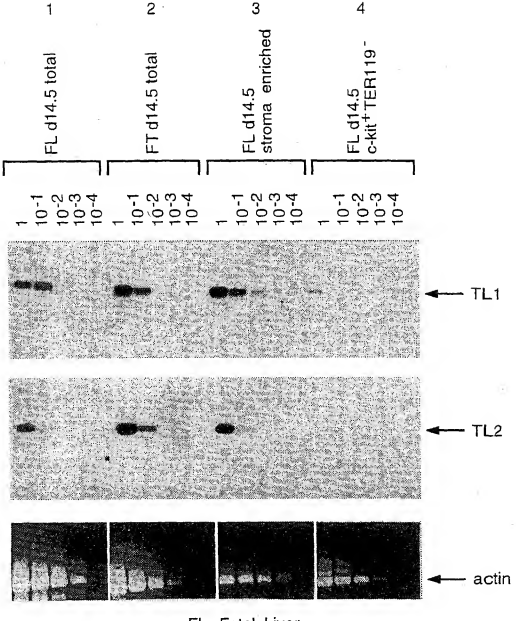
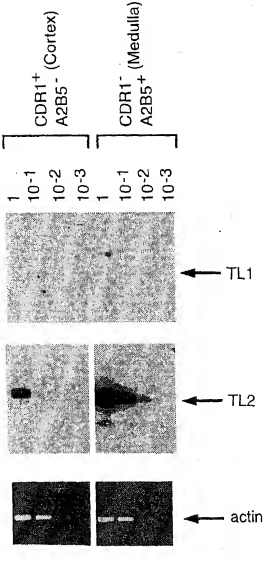


Fig.13.



FL: Fetal Liver

Fig.14.



Fetal Thymus E17.5

$CDR1^+$: Cortical stromal cells

$A2B5^+$: Medulla stromal cells

Fig.15.

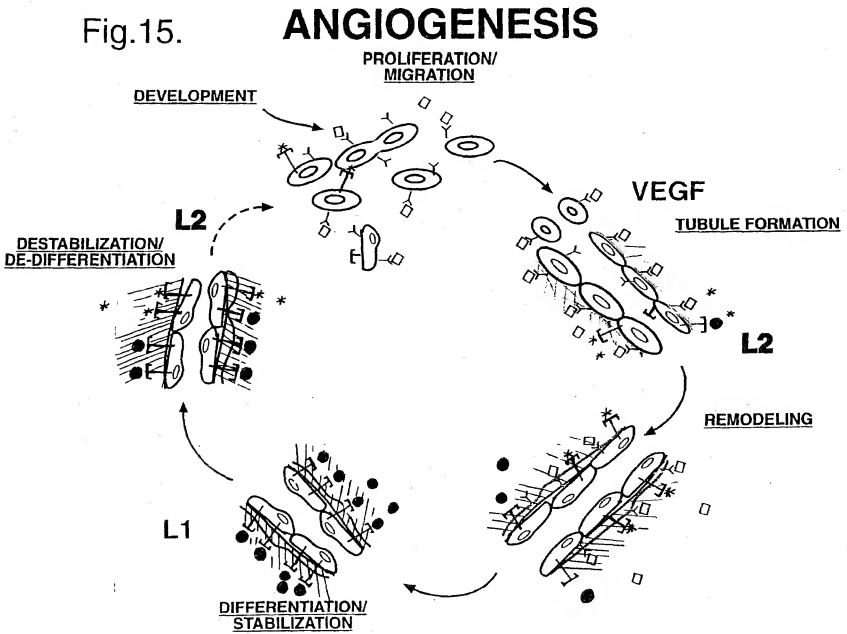


Fig.16.

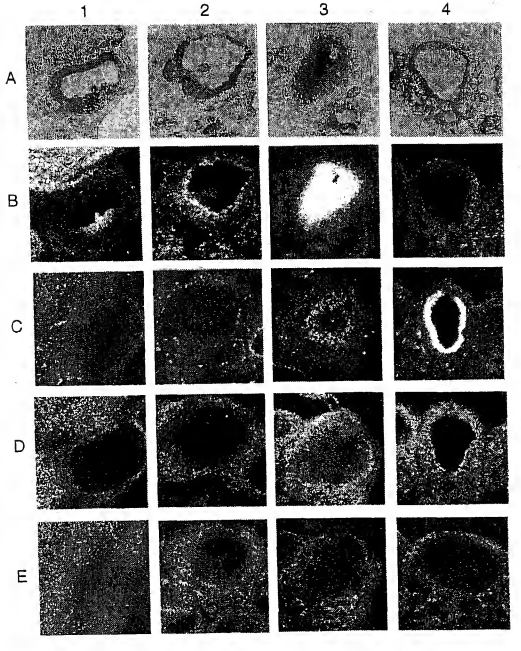


Fig.17.

ENGINEERING OF TIE2 "LIGAND-BODIES"

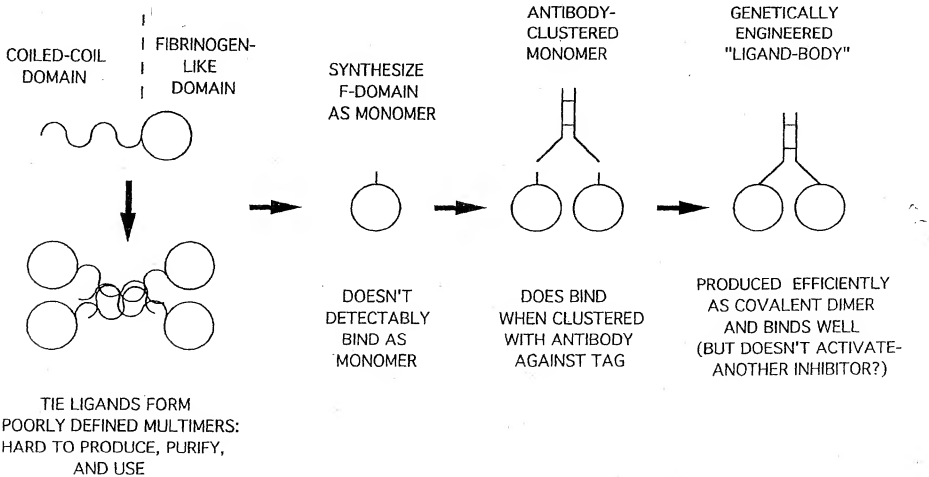


Fig.18.

COVALENT MULTIMERIC STRUCTURE OF TL1 AND TL2 AND THEIR INTERCONVERSION BY THE MUTATION OF ONE CYSTEINE

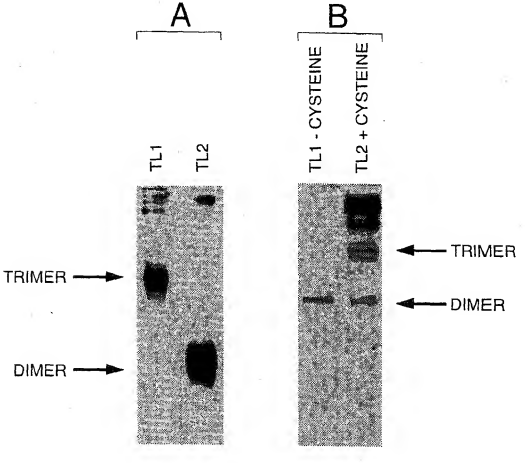


Fig.19. TIE2-IgG binding to immobilized TL1

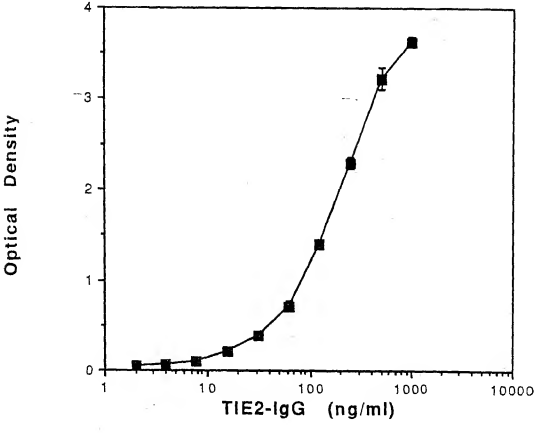


Fig.20. TL1-f-Fc binding to immobilized Tie2 ectodomain